Identification of Novel RSK-Dependent 14-3-3 Binding Proteins and Their Potential Role in Ras-MAPK Signaling.

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The Ras-MAPK signaling pathway is hyperactive in over thirty percent of human cancers and more than twice that in specific cancer types. Ribosomal S6 kinase (RSK) is involved in both positive and negative regulation in the Ras-MAPK pathway. Exploration of RSK-specific regulatory mechanisms will help illuminate an important oncogenic pathway and increase our ability to target these cancers with highly specific treatments. Previous research has identified several RSK substrates but we anticipate the elucidation of many more. RSK phosphorylates some substrates which go on to become binding partners of 14-3-3 protein. Ligature of SOS1 and 14-3-3 secondary to phosphorylation by RSK drives negative feedback in Ras-MAPK signal transduction. Through large-scale proteomics we have identified additional RSK substrates that interact with 14-3-3. In this study we provide focused assessments of two of these proteins.